THE EFFECTS OF ETHANOL ON PUNISHED RESPONDING: A COMPARISON WITH PENTOBARBITAL

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THE EFFECTS OF ETHANOL ON PUNISHED RESPONDING: A COMPARISON WITH PENTOBARBITAL

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SUMMARY

Rats were trained on a VI 90-sec multiple schedule of reinforcement. Shock was programmed to occur on an FR 3 schedule during one component of the multiple schedule. Upon stabilization of response rate, two drugs, ethanol and pentobarbital, were administered orally to the subjects every third day. On the days intervening between drug days, control solutions of sucrose and water were administered.

The results showed that certain doses of ethanol increased response rate in the punished component, but not in the unpunished component for most of the subjects. Pentobarbital produced increases in responding in the punished component for all subjects at two dose levels. In general, the magnitude of the effects on punished responding produced by pentobarbital were greater than those produced by ethanol. Pentobarbital also increased punished responding more consistently across subjects than did ethanol.

CHAPTER I

INTRODUCTION

There is much evidence indicating that behavior that has been suppressed by punishment may be increased in frequency by the administration of certain drugs. It has been well established that the benzodiazepines (Geller, Kulak & Seifter, 1962; Geller, 1964; Hanson, Witoslawski & Campbell, 1967; Goldberg & Ciofalo, 1969; Wuttke & Kelleher, 1970; Vogel, Bernard & Clody, 1971; Cannizzaro, Nigito, Provenzano & Vitikova, 1974; McMillan, 1973a, 1973b; Robichaud, Sledge, Hefner & Goldberg, 1973) and the barbiturates (Geller & Seifter, 1960; Kelleher & Morse, 1964; Morse, 1964; Hanson et al., 1967; Blum, 1970, Falk & Burnidge, 1970; Vogel et al., 1971; McMillan, 1973a, 1973b; Geller & Croy, 1974; McMillan & Leander, 1975) increase punished responding. There is also some evidence to suggest that several other drugs, including meprobamate (Geller & Seifter, 1960; Hanson et al., 1967), monourethans and di-urethans (Geller & Seifter, 1962), p-chlorophenylalanine (Robichaud and Sledge, 1969; Geller and Blum, 1970), methysergide and bromolysergic acid (Graeff, 1970), hedonal (Geller and Seifter, 1962) and cinanserin (Geller, Hartmann, Croy & Haber, 1974) may

increase punished responding. Other drugs have been shown to either increase or decrease punished responding, depending on particular factors, such as dose, rate of responding before drug administration, type of apparatus employed, shock magnitude and frequency, and schedule of punishment and reinforcement. These include reserpine (Brady, 1956; Geller, Bachman & Seifter, 1963), d-amphetamine (Geller, 1960; Hanson et al., 1967; McMillan, 1973, b; Miczek, 1973; Foree, Moretz, & McMillan, 1973), chlorpromazine (Dinsmoor & Lyons, 1963; Geller et al., 1962; Hanson et al., 1967; Martin, 1971; McMillan, 1973a, 1973b), morphine (Leaf & Muller, 1963; Geller et al., 1963; McMillan, 1973, a, b) and ethanol (Freed, 1972; Vogel-Sprott, 1967; McMillan & Leander, 1975; Hendry, 1964; Barry et al., 1963; Geller & Croy, 1974; McMillan & Leander, 1975).

Of this latter group, ethanol is certainly the most widely consumed agent. The very first written documents that have been found, clay tablets dating from about 2100 B.C., include ethanol in a wage list. A series of proper names is followed by the words: "Bread and beer for one day" (Modell & Lansing, 1967). With such a long history, it is not surprising that there is a journal, the Quarterly Journal of Studies on Alcohol, devoted entirely to the study of the effects of ethanol. And though massive amounts of data have been collected on the effects of ethanol, the behavioral effects of ethanol and, in

particular, the effects of **ethanol** on behavior suppressed by punishment have not been established with any reasonable certainty.

Ethanol is classified as a central nervous system depressant (Goodman and Gilman, 1970); however, the behavior that we often observe in persons under the influence of this drug can hardly be characterized as depressed. Verbal behavior often increases in frequency and intensity. The frequency of behaviors which could be labeled "inappropriate", "abnormal", or "excessive" increases and such behaviors are said to be "released" by the drug. But from what does ethanol release these behaviors? Perhaps ethanol releases such behaviors from the suppressive effects of punishment. If so, behaviors that have been punished by social or other means might tend to increase in frequency when an organism is under the influence of ethanol. If ethanol does increase the frequency of behaviors suppressed by punishment, then it should be possible to demonstrate the relationship in a well-controlled experimental situation.

However, the results of the experimental studies published on the effects of ethanol on punished responding have not been consistent. For example, Barry et al. (1963), using rats as subjects, alternated periods of a variable interval (VI) one-minute schedule of food delivery with periods of VI 9-second shock presentation. The VI 9-sec

shock dependency, signalled by a tone, was sometimes omitted during the tone in order to assess the effects of intraperitoneally administered ethanol on "conditioned fear". Barry et al. found that ethanol neither increased punished responding nor reduced "conditioned fear". Instead, ethanol (1.2g/kg) produced slight decreases in lever pressing in both cases. Likewise, Hendry and Van Toller (1964), using a design in which every response was reinforced with water (continuous reinforcement), found that ethanol (0.5, 1.0, 1.5, 2.0g/kg doses) administered intraperitoneally to rats decreased punished responding when shock (1.3ma) was programmed on an FR10 or FR20 schedule.

Geller and Croy (1974), using five goldfish as subjects, also failed to obtain facilitation in the rate of punished responding with ethanol, where the ethanol was taken into the subjects' systems through the solution in which they swam. Although significant increases were obtained for one goldfish at a single dose, ethanol generally had little effect upon punished responding. Geller and Croy (1974) did not specify dose levels, though blood ethanol levels were given in mg % (mg of ethanol/100 ml of blood) for three different concentrations (150, 300, and 500 mg %). In the procedure used by Geller and Croy (1974), commonly known as the Geller procedure, 3 minute periods, during which food and shock are administered for every response,

interrupt a VI 2-min schedule of reinforcement twice each hour.

Employing a similar procedure to Geller but administering ethanol orally, Freed (1972), using an unspecified dose of ethanol, obtained somewhat different results. Freed found that the rate of responding suppressed by punishment (0.5ma shock) in rats was initially increased by ethanol. In Freed's study, 20-min periods of an FI 60-sec dependency for food alternated with 3-min periods in which both shock and reinforcement were received for every response.

Vogel-Sprott (1967) found that when the same response produced both reinforcement and punishment, orally administered ethanol (0.6g/kg) increased punished responding in human subjects when the shock intensity was set at 3.55ma. However, when the shock intensity was 2.55ma and responding was little depressed, punished responding was not significantly increased by ethanol.

A recent study by McMillan and Leander (1975), has demonstrated that a 1g/kg dose of ethanol administered orally to pigeons can increase FI 5-min responding suppressed by an FR 1 schedule of response-dependent shock. This same responding was decreased by a 2g/kg dose of ethanol, while a 0.5g/kg dose had no effect. Each of three pigeons received a single gastric intubation of each dose of ethanol. In the study, each of the remaining three pigeons were yoked to one of the first three birds such

that each received response-independent shock at the same time as the first three birds received response-dependent shock. Responding suppressed by response-independent shock was further decreased by all three doses of ethanol. In the same study, pentobarbital injected intramuscularly increased responding suppressed by response-dependent shock for a 10mg/kg dose and by response-independent shock in 3, 5.6, and 10mg/kg doses. Responding was decreased for both response-dependent and response-independent shock for the 17.5mg/kg dose of pentobarbital.

In general, pentobarbital has been shown to increase punished responding in widely differing experimental designs. In fact, in every study employing pentobarbital reviewed by the author, pentobarbital was shown to increase punished responding (Geller & Seifter, 1960; Geller & Seifter, 1962; Keller & Morse, 1964; Hanson et al., 1967; Vogel, 1971; McMillan, 1973a, 1973b; Blum, 1970; Falk & Burnidge, 1970; McMillan & Leander, 1975).

Pentobarbital shares many pharmacological properties with ethanol. Both ethanol and pentobarbital are classified as central nervous system depressants, demonstrate anti-convulsant properties, and exhibit effects on the reticular system of the brain. In addition, ethanol and pentobarbital produce similar patterns of intoxication, may lead to physical dependence, and produce similar withdrawal symptoms. Furthermore, either drug

may substantially suppress the withdrawal symptoms produced by the other (Goodman and Gilman, 1970). Although ethanol has traditionally been considered to reduce pain, neither ethanol nor pentobarbital has significant analgesic effects at low doses (Siegmund, 1957; Hendershot & Forsaith, 1959). Since the pharmacological properties of the two drugs are similar, it is reasonable to expect the behavioral effects of the drugs also to be similar. By comparing the effects of ethanol on punished responding with those of pentobarbital, it may be ascertained if certain behavioral effects are indeed similar.

CHAPTER II

CRITICISM OF PREVIOUS APPROACHES AND RATIONALE FOR PRESENT STUDY

For the six studies reviewed relating to the effects of ethanol on punished responding (McMillan & Leander, 1975; Geller & Croy, 1974; Freed, 1972; Vogel-Sprott, 1967; Hendry & Van Toller, 1964; Barry et al., 1963), three obtained increases in punished responding, while the other three failed to obtain this effect. What can account for these discrepancies? And what are the procedural changes necessary to arrive at a somewhat firmer conclusion with respect to the effects of ethanol on punished responding?

Freed (1972), Vogel-Sprott (1967) and McMillan and Leander (1975) all obtained increases in punished responding, and all administered ethanol orally. In contrast, Barry et al. (1963) and Hendry and Van Toller (1964), who failed to obtain increases in punished responding, each administered ethanol intraperitoneally. In another study, Geller and Croy (1974), increases were generally not obtained. In that study the ethanol was absorbed directly into the blood from the solution in which the goldfish swam. The testing was conducted after the ethanol concentration in the subjects' blood rose to a level equal to that of the

liquid in which they were submerged.

But why should the route of drug administration make any difference? The answer may lie in differentially achieved blood ethanol levels. The peak blood ethanol concentration is determined not only by dose, but by the method of drug administration (Fish & Nelson, 1942). The rate at which the blood ethanol level rises also varies with the route of drug administration. Fish and Nelson (1942) compared oral vs. intraperitoneal (IP) administration of ethanol in rats. Although a 2.5g/kg dose was the only dose for which the two routes of administration were compared, the results are enlightening. Following drug administration, ethanol concentration in the blood was measured periodically over a period of four and one-half hours. For the oral group, the average blood concentration after 30 minutes was 134 mg per 100 ml of blood (134mg %). In contrast, the blood concentration in the injected group rose to more than 280 mg % in 15 minutes and by the end of 30 minutes, the ethanol blood concentration stood at 286 mg %. This concentration is more than twice the concentration after the same length of time for the same dose of ethanol administered orally. At the end of 60 minutes, the ethanol concentration for the injected rats was still more than twice that for the oral group. The average ethanol blood concentration of rats given a 2.5g/kg dose orally during a 60 minute period was 133 mg %.

Compare this to an average blood concentration (136 mg %) over the same time period for rats given a 1.25g/kg dose intraperitoneally. Thus for a 60-minute session, the average blood concentration for a 1.25g/kg dose administered IP is practically equal to that for a 2.5g/kg dose administered orally.

Now consider the Barry et al. (1963) study in which rats were injected IP with 1.2g/kg of ethanol. The length of the sessions was 12 minutes and ethanol was given 20 minutes prior to each session. From the data given by Fish and Nelson (1942), an estimate of the blood level in the Barry et al. (1963) study is about 150 mg %.

Geller and Croy (1974) measured blood ethanol levels of 150, 300 and 500 mg %. Compare these levels of blood ethanol to the 50 to 30 mg % level present in the Vogel-Sprott (1967) study. It is possible that the lower blood ethanol level in the Vogel-Sprott study was responsible for the increases obtained in punished responding in that study. McMillan and Leander (1975) obtained increases in punished responding with a 1g/kg oral dose of ethanol. This oral dose could be expected to produce lower blood ethanol levels than the 1.2g/kg IP dose given by Barry et al. (1963). In line with this analysis, McMillan and Leander (1975) found that a 2g/kg dose of ethanol further decreased punished responding.

Thus only low doses of ethanol administered orally were shown to increase punished responding in the studies reviewed (McMillan & Leander, 1975; Geller & Croy, 1974; Freed, 1972; Vogel-Sprott, 1967; Hendry & Van Toller, 1964; Barry et al., 1963). This result would imply that a wide range of doses of ethanol, including several low doses, should be administered orally to assess more thoroughly the effects of ethanol on punished responding. None of the studies reviewed used a wide range of low doses administered orally. In addition, none of the studies reviewed administered the same dose to any subject more than once. Multiple administrations at each dose level would seem advantageous in order to draw conclusions about the relationship between dose level and punished responding.

At least one more aspect of the ethanol-punishment studies mentioned merits discussion. In all of the studies reviewed (McMillan & Leander, 1975; Geller & Croy, 1974; Freed, 1972; Vogel-Sprott, 1967; Hendry & Van Toller, 1964; Barry et al., 1963) punishment was often paired with reinforcement. In a design in which any single lever press on occasion produces both food and shock, the shock may act not only as a punisher but also as a discriminative stimulus for food presentation and a conditioned reinforcer. Although there is no evidence one way or the other that simultaneously reinforcing and punishing the same response

modifies the effects of drugs on punished responding, it would seem conceptually that a punishing stimulus should have a minimum of additional properties.

The purpose of the present study is to determine the effects of ethanol on punished responding. To achieve this purpose, the study is somewhat broader in scope than previous research, while retaining some of the desirable features of this research. A wide range of doses of ethanol is employed and each of these doses is administered twice. The contingencies of reinforcement and punishment are programmed such that the punishing stimulus is never directly paired with reinforcement. Thus, shock cannot itself signal that food is forthcoming. In two studies, Geller and Croy (1974) and McMillan and Leander (1975), ethanol and barbiturates were both administered. This procedure allows the relative magnitude of the effects of the two drugs to be assessed. This is especially true in the case of the present experiment, in which effects produced by a wide range of doses of both ethanol and pentobarbital are compared. In addition, ethanol is administered "orally", retaining the method of drug administration employed by the studies (McMillan & Leander, 1975; Freed, 1972; Vogel-Sprott, 1967) successful in showing increases in punished responding following ethanol administration.

CHAPTER III

METHOD

Subjects

Four male Charles River rats derived from the Sprague Dawley strain and of approximately the same weight and age were used. The animals were about 90 days old at the start of the experiment. They were reduced to 75% of their free-feeding weight and maintained at this weight throughout the experiment.

Apparatus

The apparatus consisted of a transparent plexiglass experimental chamber equipped with a lever, which could be pressed with a minimum force of .38N. to obtain 97mg sucrose pellets. Mounted on the same wall of the experimental chamber to the right of the lever was a small white light. Fixed on each of the two walls adjacent to the lever was a loudspeaker. Shock was provided by a Grayson-Stadler E1064GS shock generator and was administered to the rat via the lever and the grid floor of the experimental chamber. The experimental chamber, located in a larger, opaque, sound-attenuated chamber, was controlled by relay programming equipment in an adjacent room. Mounted on the wall of the larger chamber was a 15-watt houselight.

Recording apparatus included a Ralph Gerbrands cumulative recorder, impulse counters and timers. In addition to the standard equipment, a Perfektum stainless steel, 16 guage tube with a 3mm ball attached to a plastic 10cc syringe was used for oral drug administration.

Procedure

The lever-pressing response was shaped by reinforcing successive approximations to the desired response with sucrose pellets. After acquiring the lever-pressing response, the subjects were exposed to a number of sessions wherein each response was followed by the presentation of a sucrose pellet (CRF schedule). The subjects were then trained on a multiple variable-interval (VI) schedule of reinforcement. A variable-interval schedule of reinforcement arranges for reinforcer availability following a variable interval of time. The first response following this variable interval is reinforced. The value of the VI schedule is the mean value of all the intervals making up the schedule. In the present study the VI parameter value was increased from 30 seconds the first day to 60 seconds the next five days and finally to 90 seconds for the remainder of the experiment.

A multiple VI VI schedule of reinforcement can be thought of as comprising two independent VI schedules, which alternate in time. For each of the independent VI schedules,

a different set of stimulus conditions exists. Each independent VI schedule will henceforth be referred to as a "component" of the multiple schedule.

In the present experiment, subsequent to the shaping procedure and initial training, a multiple VI 90-sec VI 90-sec schedule for food reinforcement was employed. The 30 interval values (360, 55, 61, 270, 73, 6, 9, 20, 126, 3, 36, 88, 80, 27, 23, 225, 195, 154, 105, 32, 139, 45, 67, 13, 16, 50, 40, 172, 96, 115) that comprised each component of the multiple VI 90-sec VI 90-sec schedule were calculated by using the constant probability equation given by Catania and Reynolds (1968). During one of the components of the VI 90-sec VI 90-sec schedule, the small white light was illuminated and white noise was present. During the other component, a 1000 Hz. tone was superimposed upon the white noise and the white light was off. The VI 90-sec components alternated every five minutes. Thus, during each five minute component, the animals could obtain an average of three pellets. The duration of each experimental session was sixty minutes. The 15-watt houselight was switched on to signal the start of the 60-minute session and remained on for the duration of each session. An experimental session was conducted each week day. During the latter part of the experiment, weekend sessions were also conducted.

The rats were trained on the multiple schedule until the response rate became stable. Stability was defined as

a coefficient of variation of no more than 15% over a five-session block. The mean response rate of the first five session block during which responding was stable was designated as the pre-shock baseline.

After the response rate had stabilized for each animal, electric shock was introduced into the component of the multiple schedule signalled by the 1000 Hz. tone and the offset of the small white light. The shock was programmed on a fixed-ratio (FR 3) schedule. During this punishment component shock was arranged to occur following every third lever press unless that lever press produced a sucrose pellet according to the VI 90-sec reinforcement schedule. Whenever the lever press produced reinforcement, the response counter for shocks did not advance and shock did not occur. The shock was thus delayed until a lever press was executed that did not produce a reinforcer. Therefore punishment was explicitly not paired with reinforcement, though both shock and food were dependent on lever pressing. The shock was initially set at a low intensity (.05ma) and was gradually increased in intensity until the rate of responding during the punished component stabilized at about 25% of the unpunished pre-shock baseline rate. With this procedure, the rate of punished responding may vary in either direction (McMillan, 1973 a), while response rate in the punished component is decreased to the extent that the effects of the shock dependency are clearly visible. The

final shock intensities for R9, R10, R11 and R12 were 0.25, 0.25, 0.20 and 0.30ma, respectively. The shock duration was set at 0.5 seconds throughout the experiment.

When the rate of responding in the punished component began to reach a level approximately equal to 25% of the pre-shock baseline rate, the intubation procedure was introduced. The intubation procedure involved holding the animal as steady as possible, while delivering a drug or control solution into the animal's stomach via the metal tube inserted into the animal's esophagus. All animals were initially intubated with a sucrose solution in order to allow them to adapt to the intubation procedure. For the next several weeks, a 1g/kg sucrose solution was administered. Meanwhile, the response rate was monitored in order to determine whether or not responding had stabilized.

Upon stabilization of punished responding, ethanol was administered orally to subjects R11 and R12 in 0.5, 0.75, 1.0, 1.25, 1.5, 2.0, 2.5, and 4.0g/kg doses beginning with the lowest dose. Following the ethanol regimen, pentobarbital was administered to these same subjects in 8, 10, 12, 16 and 20mg/kg doses. The order of administration of ethanol and pentobarbital are shown in Table 1.

The other two subjects, R9 and R10, were given pentobarbital first in 8, 10, 12, 16 and 20mg/kg doses, followed by ethanol in 0.5, 1.0, 1.5, 2.0, 2.5 and 4.0g/kg doses. Both drugs were initially administered in the order of

Table 1. Sequence of Ethanol and Pentobarbital Administration

	Ethanol Dose (g/kg)				Pentobarbital Dose (mg/kg)			
Subject	R9	R10	R11	R12	R9	R10	R11	R12
Drug Day								
1	0.5	0.5	0.5	0.5	8	8	8	8
2	1.0	1.0	0.75	0.75	10	10	10	10
3	1.5	1.5	1.0	1.0	12	12	12	12
4	2.0	2.0	1.25	1.25	16	16	16	16
5	2.5	2.5	1.5	1.5	20	20	20	20
6	4.0	4.0	1.5	1.5	20	20	20	20
7	4.0	4.0	1.25	1.25	16	16	16	16
8	2.5	2.5	1.0	1.0	12	12	12	12
9	2.0	2.0	0.75	0.75	10	10	10	10
10	1.5	1.5	0.5	0.5	8	8	8	8
11	1.0	1.0	2.0	2.0				
12	0.5	0.5	2.5	2.5				
13			4.0	4.0				
14			4.0	4.0				
15			2.5	2.5				
16			2.0	2.0				

ascending dose levels and then in descending order.

All four subjects received a 3cc solution of each drug mixed with water every third day. The concentration of the ethanol solution ranged from 7 to 70 percent (w/v). The pentobarbital concentrations ranged from 0.08 to 0.2 percent (w/v). Subjects receiving ethanol were given a 3cc sucrose solution that was isocaloric to the preceding ethanol dose as a control on the two intervening days. For those subjects receiving pentobarbital, water was intubated on the two non-drug days. All solutions, drug and control were administered orally fifteen minutes prior to the beginning of each session. Each subject received each drug dose twice over the course of the experiment.

The administration of the drugs every third day, coupled with the use of low doses of each drug should have prevented significant tolerance from developing. Studies that have demonstrated the development of tolerance to ethanol (Le Blanc, Kalant, & Gibbons, 1969; Hatfield, 1972; Le Blanc, & Kalant, 1973) and to pentobarbital (Yanagita & Takahashi, 1970; Aston, 1965) have typically used high doses and a daily schedule of drug administration.

A continuous record of the subject's lever presses over time was recorded using a Ralph Gerbrands cumulative recorder. The occurrence of each shock was also indicated by the recorder. Supplementing this continuous record, the total number of lever presses was accumulated separately

by impulse counters for each component of the multiple schedule, as was the number of sucrose pellets delivered in each component. The total number of shocks taken by each subject was also recorded by an impulse counter. Timers recorded the total time of each component for an experimental session.

A measure of the distribution of times between successive lever presses (interresponse times) was also obtained. Interresponse times (IRT's) have been shown to provide orderly data describing schedule performance (Morse, 1966) and to be sensitive to drug effects (Schuster, Dockens, & Woods, 1960). The IRT's were recorded by means of two banks of ten counters each. One bank of ten counters recorded IRT's in the punished component, while the other bank recorded unpunished IRT's.

CHAPTER IV

RESULTS

Pre-shock Baseline

The response rate of all subjects stabilized on the multiple VI 90-sec VI 90-sec schedule. The coefficients of variation ranged from 5.43% to 14.9%. The means and standard deviations of this pre-shock baseline are given in the Table 2. Following stabilization of responding in the pre-shock condition, shock was introduced into the component signalled by the light offset and the 1000 Hz. tone. The introduction of shock and the systematic increase in shock intensity gradually decreased response rate in the punished component of the multiple schedule. The rate of responding in the punished component for all subjects was decreased such that response rate for each subject at the final shock level averaged between 17 and 25 percent of the unpunished pre-shock baseline rate. The average rate in the unpunished component varied from about 56% of the pre-shock rate for R10 to about 196% for R12. The means and standard deviations of the response rate in the punished and unpunished components for the final shock levels are given in Table 3. The response rates in Table 3 are presented in terms of percent of the pre-shock

Table 2. Pre-shock Baseline Response Rate Means & S.D.'s

	Light-off Component		Light-on Component	
Subject	$\bar{X}$	S.D.	$\bar{X}$	S.D.
R9	3.446	0.342	3.744	0.529
R10	24.574	1.65	25.858	3.84
R11	10.81	1.2028	11.738	0.6378
R12	4.06	0.535	4.32	0.399

Table 3. Response Rates for Final Shock Intensity Level Prior to Drug Regimen

Subject	Shock Level	Punished Rate in % of Preshock Rate $\bar{X}$	Punished Rate in % of Preshock Rate S.D.	Unpunished Rate in % of Preshock Rate $\bar{X}$	Unpunished Rate in % of Preshock Rate S.D.
R9	.25ma	19.57	6.02	172.46	57.51
R10	.25ma	17.76	4.59	55.89	13.00
R11	.20ma	17.32	3.69	80.357	15.78
R12	.30ma	25.36	7.47	195.91	53.98

baseline levels.

Pre-Drug Baseline

For subjects R11 and R12, response rate stabilized. The coefficients of variation ranged from 5% to 14%. The coefficients of variation for all subjects for the last 5-session block before the drug regimen began are shown in Table 4. For subjects R9 and R10, response rate had not stabilized after 6 weeks at the final shock level. A coefficient of variation less than 15% was not obtained for these subjects. Since response rate did not stabilize for these two subjects, it was decided that the best baseline against which to assess drug effects for all subjects consisted of the response rate on the control days immediately preceding each drug dose.

Number of Reinforcements Received

During a 60-minute session each subject could obtain a maximum of about 40 reinforcements, 20 per component. The variable interval schedule permits response rate to vary widely without affecting the number of reinforcements obtained. However in the punished component, the response was often very low, such that less than 20 reinforcements were obtained in the punished component. The average number of reinforcements obtained in the punished component for the pre-drug control days for subjects R9, R10, R11 and R12 were approximately 14, 17, 16 and 14,

Table 4. Coefficients of Variation for Last 5-Session Block Before Drug Regimen

	Coefficients of Variation	
Subject	Punished Component	Unpunished Component
R9	18%	29%
R10	4%	27%
R11	11%	10%
R12	5%	14%

respectively. The average number obtained in the unpunished component for R9, R10, R11 and R12 were 20, 20, 21 and 20 reinforcements, respectively.

Number of Shocks Received

The mean number of shocks received by each subject following pentobarbital administration at various doses and the mean and standard error for the shocks received on the corresponding water control days are shown in Table 5. As Table 5 shows, doses of 8, 10, 12 and 16mg/kg of pentobarbital produced increases in the number of shocks received by three of four subjects. The 8 and 16mg/kg doses produced no effects on the number of shocks received by R10. The 20mg/kg dose produced increases in number of shocks received for R9 and decreases for R11. This dose had no effect for subjects R10 and R12.

Table 6 compares the mean number of shocks received following each dose of ethanol with the mean of the sucrose control days. For subjects R11 and R12, increases in the number of shocks received were obtained following administration of 2.0 and 2.5g/kg doses. In addition, R9 received an increase in number of shocks following the 1.0 g/kg dose of ethanol. Decreases were observed at the 4.0 g/kg dose for R10 and at the 1.25g/kg dose for R12. No other dose of ethanol produced effects on the number of shocks received for any other subject.

Table 5. Mean Number of Shocks Received Per Session - Pentobarbital Regimen

Subject	R9	R10	R11	R12
	(n=10)	(n=10)	(n=10)	(n=10)
Control	$\bar{X}_c \pm 2S.E.$	$\bar{X}_c \pm 2S.E.$	$\bar{X}_c \pm 2S.E.$	$\bar{X}_c \pm 2S.E.$
	6.4 ± 3.2	46.1 ± 22.3	32.6 ± 11.3	9.2 ± 4.0
Drug Dose (mg/kg)	(n=2)	(n=2)	(n=2)	(n=2)
8	15.5*	55	54.5*	16*
10	16*	75*	53*	18.5*
12	26.5*	77.5*	45.5*	33.5*
16	22*	58	47*	32.5*
20	27*	27.5	5.5*	7.5

* Indicates that the average number of shocks at a particular dose of pentobarbital is more than two standard errors from the control mean.

Table 6. Mean Number of Shocks Received Per Session - Ethanol Regimen

Subject	R9	R10	R11	R12
	(n=12)	(n=12)	(n=16)	(n=16)
Control	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$
	9.7 ± 6.0	51.6 ± 31.2	26.2 ± 6.6	7.4 ± 2.5
Drug Dose (g/kg)	(n=2)	(n=2)	(n=2)	(n=2)
.50	14.5	65	27.5	8
.75	-	-	23.5	7.5
1.0	16.5*	46	22.5	7.5
1.25	-	-	26.5	4.5*
1.50	14	49	29.5	6.5
2.0	15	42.5	45.5*	16*
2.5	12	44.5	37.5*	11*
4.0	8.5	15.5*	31.5	7

* Indicates that the average number of shocks at a particular dose of ethanol is more than two standard errors from the control mean.

A drug/control shock ratio was computed for each dose of pentobarbital. The ratio was computed by dividing the mean number of shocks taken at a particular dose of pentobarbital by the mean number of shocks received on the water control days. For the ten control days preceding the ten pentobarbital administrations, a mean and standard error were computed. If pentobarbital did not produce changes in punished responding, the drug/control shock ratio would equal 1.0. Small deviations of this ratio from unity, however, cannot necessarily be attributed to drug effects due to small day-to-day fluctuations in response rate. To account for these random fluctuations, quasi-confidence bands were calculated using the standard error of the control mean for number of shocks. The "confidence bands" were calculated by the following formula:

$$\text{Upper \& Lower Quasi-Confidence Bands} = \frac{\bar{S}c \pm 2S.E.}{\bar{S}c} \qquad (1)$$

$\bar{S}c$ denotes the mean number of shocks received on the control days and S.E. is the standard error of this mean. The average drug/control shock ratios for each dose of pentobarbital are given in Table 7. Ratios falling outside of the "confidence bands" indicate drug-produced effects and are marked with astericks in the table. Table 8 contains

Table 7. Average Drug/Control Shock Ratios - Pentobarbital

Subject	R9	R10	R11	R12
Dose Level (mg/kg)				
8	2.42*	1.19	1.67*	1.74*
10	2.5*	1.63*	1.63*	2.01*
12	4.14*	1.68*	1.40*	3.64*
16	3.44*	1.26	1.44*	3.53*
20	4.22*	0.60	0.17*	0.82

* Denotes a drug effect on the number of shocks taken by a subject at a particular dose, as defined by ratios exceeding the upper or lower quasi-confidence bands.

the average drug/control shock ratios for ethanol. As in Table 7, ratios exceeding the "confidence limits" are indicated by astericks. The results in Tables 7 and 8 are identical to those in Tables 5 and 6. However, the data in Tables 7 and 8 permit a direct comparison of the relative magnitude of the effects of pentobarbital and ethanol. In general, the drug/control shock ratios are larger for pentobarbital than for ethanol. In addition, fewer doses of ethanol produced "significant" ratios. For subject R10, no effects were noted with ethanol, but pentobarbital produced "significant" ratios of 1.63 and 1.68.

Effects of Pentobarbital and Ethanol on Punished Responding

The mean number of shocks received by each subject in the punished component is one index of punished responding. A closely related index of punished responding is the response rate in the punished component. In Table 9, the mean response rates of each animal following pentobarbital administration are given in responses per minute. In addition, punished mean response rates and standard errors are given for the water control days. Table 10 presents the same information for the various ethanol and sucrose doses. As shown in Table 9, response rate in the punished component was increased by 8, 10, 12 and 16 mg/kg doses of pentobarbital for three of four subjects. For subject R10, the only pentobarbital effects were increases following 10

Table 8. Average Drug/Control Shock Ratios - Ethanol

Subject	R9	R10	R11	R12
Dose Level (g/kg)				
.50	1.49	1.26	1.05	1.08
.75	-	-	0.90	1.01
1.0	1.70*	0.89	0.86	1.01
1.25	-	-	1.01	0.61
1.50	1.44	0.95	1.13	0.88
2.0	1.55	0.82	1.74*	2.16*
2.5	1.24	0.86	1.43*	1.49*
4.0	0.88	0.30*	1.20	0.95

* Denotes a drug effect on the number of shocks taken by a subject at a particular dose, as defined by ratios exceeding the upper or lower quasi-confidence bands.

and 12mg/kg doses. The 20mg/kg dose increased response rate suppressed by punishment for R9, but decreased the rate for subjects R11 and R12.

Ethanol moderately increased punished response rate at the 2.0g/kg dose for subjects R11 and R12, and produced a very small increase at the 1.0g/kg dose in rate for R9. The 2.5g/kg dose also produced moderate increases in rate for subjects R11 and R12. The 4.0g/kg dose produced decreases in punished rate for R10, but had little effect for other subjects.

A drug/control response rate ratio was computed by dividing the mean response rate over the two sessions at each drug dose by the mean rate of control sessions. As for the drug/control shock ratios, "confidence bands" were computed by using the standard error of the mean of the control days. The formula given below was used to calculate the quasi-confidence bands.

$$\text{Upper \& Lower Quasi-Confidence Bands} = \frac{\bar{r}c \pm 2S.E.}{\bar{r}c} \qquad (2)$$

The symbol $\bar{r}c$ denotes the mean control response rate in the punished component and S.E. denotes the standard error of this mean. The drug/control response ratios are shown in Table 11 for pentobarbital and in Table 12 for ethanol.

Table 9. Mean Response Rates (Responses/Min.) in the Punished Component - Pentobarbital Regimen

Subject	R9	R10	R11	R12
	(n=10)	(n=10)	(n=10)	(n=10)
Control	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$
	1.10 ± 0.34	5.20 ± 2.31	3.81 ± 1.16	1.42 ± 0.38
Drug Dose (mg/kg)	(n=2)	(n=2)	(n=2)	(n=2)
8	2.10*	6.04	5.99*	2.20*
10	2.10*	8.08*	5.93*	2.33*
12	2.98*	8.39*	5.21*	3.91*
16	2.80*	6.52	5.21*	3.95*
20	3.34*	3.08	0.67*	0.90*

* Indicates that the mean response rate at a particular dose of pentobarbital is more than two standard errors from the mean control rate.

Table 10. Mean Response Rates (Responses/Min.) in the Punished Component - Ethanol Regimen

Subject	R9	R10	R11	R12
	(n=12)	(n=12)	(n=16)	(n=16)
Control	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$
	1.45 ± 0.675	5.65 ± 3.04	2.83 ± 0.62	1.21 ± 0.29
Drug Dose (g/kg)	(n=2)	(n=2)	(n=2)	(n=2)
0.5	1.98	7.09	3.38	1.32
0.75	-	-	3.16	1.25
1.0	2.13*	5.25	2.86	1.21
1.25	-	-	3.23	0.97
1.50	1.92	5.41	3.67	1.15
2.0	2.0	4.84	5.35*	2.24*
2.5	1.69	5.03	4.42*	1.62*
4.0	1.24	1.93*	3.75	1.15

* Indicates that the mean response rate at a particular dose of ethanol is more than two standard errors from the mean control rate.

Asterisks in these tables indicate those doses producing effects exceeding the confidence bands. Effects as shown in Tables 11 and 12 are identical to those for the rate data in Tables 9 and 10. Figure 1 shows the mean drug/control response ratios in the punished component at each dose of pentobarbital for R11. Figure 2 illustrates the corresponding drug/control ratios for ethanol for the same animal. A comparison of those figures illustrates that pentobarbital produces a larger increment than ethanol in responding suppressed by punishment. The differences in the magnitude of effects produced by pentobarbital and those produced by ethanol were as large or larger for the remaining subjects, as can be seen by comparing the ratios in Tables 11 and 12.

Effects of Pentobarbital and Ethanol on Unpunished Responding

Response rates in the unpunished component of the multiple schedule are given for ethanol in Table 13 and for pentobarbital in Table 14. No dose of ethanol produced increases in unpunished responding. Decreases were observed for the 4.0g/kg dose for subjects R10, R11 and R12. Additional decreases were found for R11 at the 1.0g/kg dose and for R9 at the 2.5g/kg dose. However, as shown in Table 14, pentobarbital produced rate increases for R12 at the 12 and 16mg/kg doses. For all other subjects, the doses of pentobarbital that increased punished responding failed to

Table 11. Average Drug/Control Response Ratios in the Punished Component - Pentobarbital Regimen

Subject	R9	R10	R11	R12
Dose Level (mg/kg)				
8	1.90*	1.16	1.57*	1.55*
10	1.90*	1.55*	1.56*	1.64*
12	2.71*	1.61*	1.37*	2.75*
16	2.55*	1.25	1.37*	2.78*
20	3.04*	0.59	0.18*	0.63*

* Denotes a drug effect on the response rate for a subject at a particular dose, as defined by ratios exceeding the upper or lower quasi-confidence bands.

Table 12. Average Drug/Control Response Ratios in the Punished Component - Ethanol Regimen

Subject	R9	R10	R11	R12
Dose Level (g/kg)				
0.5	1.37	1.25	0.95	1.09
0.75	-	-	0.99	1.03
1.0	1.47*	0.93	0.89	1.0
1.25	-	-	1.01	0.80
1.50	1.32	0.96	1.15	0.95
2.0	1.38	0.86	1.67*	1.85*
2.5	1.17	0.89	1.38*	1.34*
4.0	0.86	0.34*	1.17	0.95

* Denotes a drug effect on the response rate for a subject at a particular dose, as defined by ratios exceeding the upper or lower quasi-confidence bands.

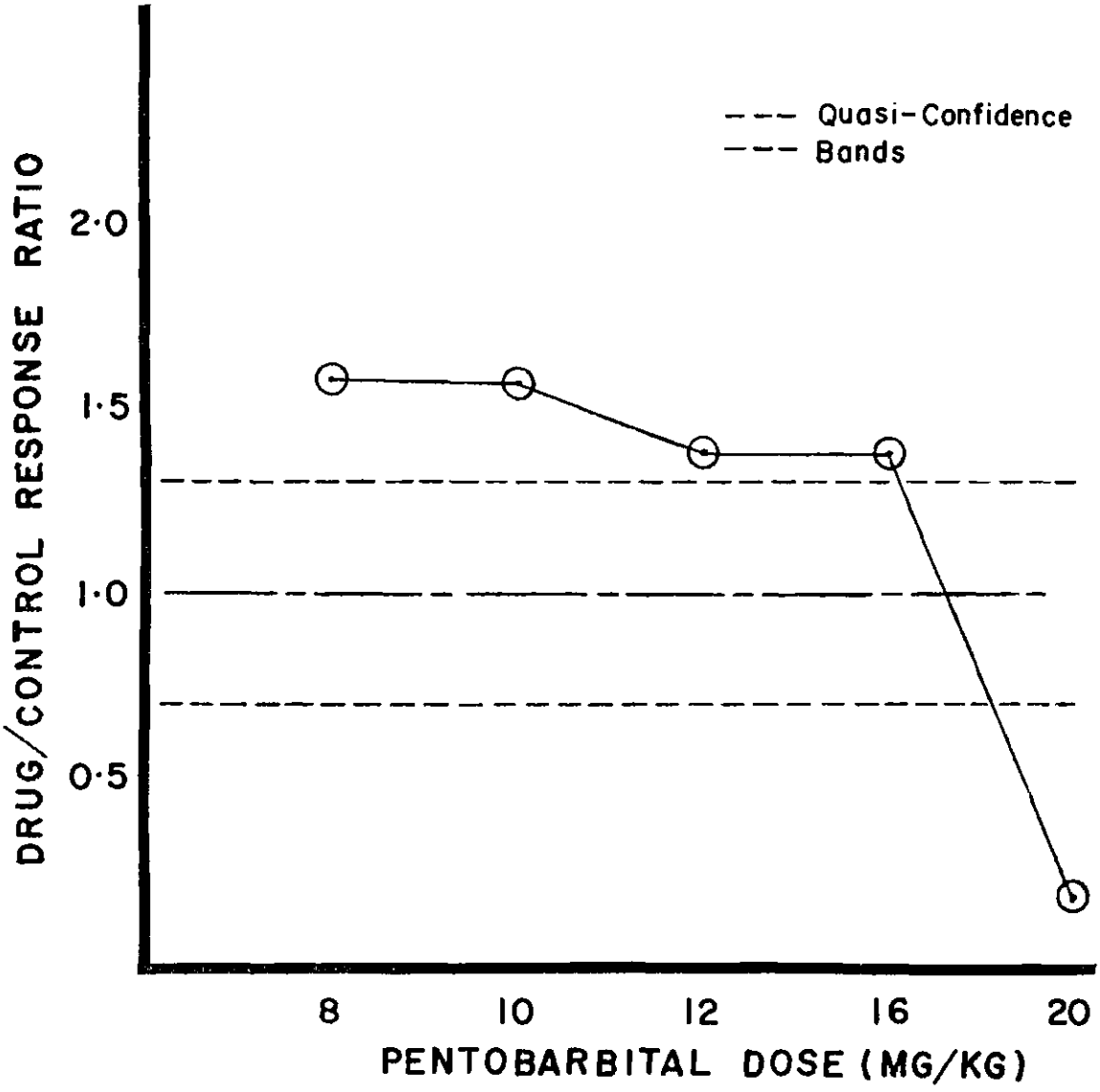

Figure 1· Drug/Control Response Ratio in the Punished Component for Subject RII– Pentobarbital Regimen

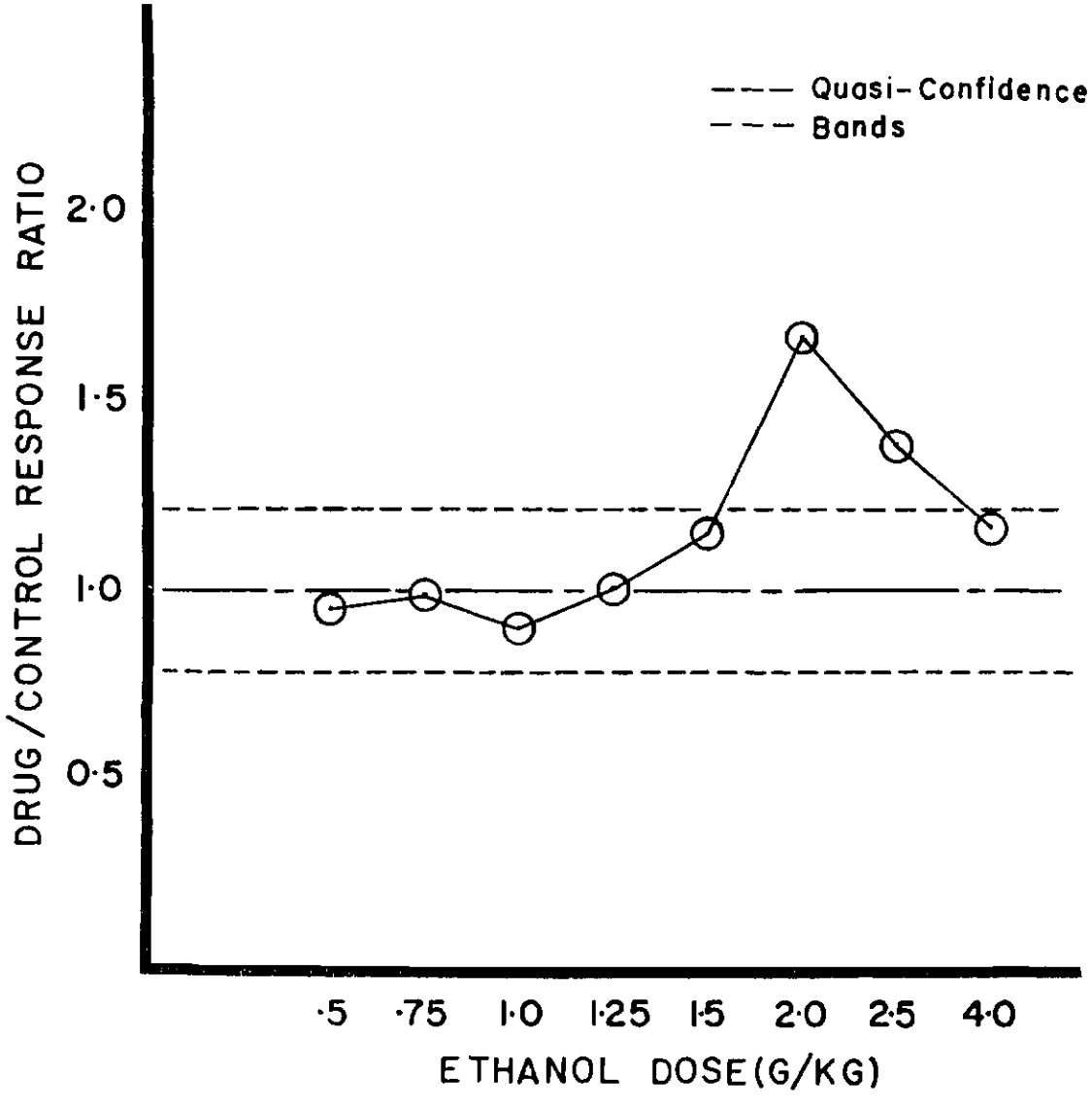

Figure 2· Drug/Control Response Ratio in the Punished Component for Subject RII- Ethanol Regimen

Table 13. Mean Response Rates (Responses/Min.) in the Unpunished Component - Ethanol Regimen

Subject	R9	R10	R11	R12
	(n=12)	(n=12)	(n=16)	(n=16)
Control	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$
	8.95 ± 3.58	9.77 ± 5.61	10.34 ± 3.41	7.53 ± 3.23
Drug Dose (g/kg)	(n=2)	(n=2)	(n=2)	(n=2)
0.5	8.35	11.56	8.58	8.67
0.75	-	-	8.0	7.45
1.0	8.10	12.34	5.81*	5.0
1.25	-	-	8.44	5.43
1.5	9.09	9.39	10.7	6.78
2.0	7.10	9.33	8.64	6.67
2.5	3.83*	7.75	8.11	4.47
4.0	5.42	2.45*	6.86*	2.60*

* Indicates that the mean response rate at a particular dose of ethanol is more than two standard errors from the control mean.

Table 14. Mean Response Rates (Responses/Min.) in the Unpunished Component - Pentobarbital Regimen

Subject	R9	R10	R11	R12
	(n=10)	(n=10)	(n=10)	(n=10)
Control	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$	$\bar{X}c \pm 2S.E.$
	5.59 ± 3.79	12.83 ± 7.69	9.51 ± 4.05	9.12 ± 3.43
Drug Dose (mg/kg)	(n=2)	(n=2)	(n=2)	(n=2)
8	5.13	13.40	11.02	10.81
10	5.18	18.59	8.33	9.2
12	7.27	13.17	8.64	14.08*
16	4.64	8.12	6.30	16.01*
20	3.43	2.7*	0.69*	2.66*

* Indicates that the mean response rate at a particular dose of pentobarbital is more than two standard errors from the control mean.

increase unpunished responding.

Tables 15 and 16 give drug/control response ratios in the unpunished component for ethanol and pentobarbital, respectively. "Confidence bands" were calculated using formula 2. Ratios exceeding the limits defined by the "confidence bands" are indicated by asterisks in the tables. The only effects observed following ethanol were decreases in rate as indicated by ratios exceeding the lower confidence band less than one. For pentobarbital, increases in rate, indicated by ratios exceeding the upper confidence band, were observed for R12. Ratios of unpunished rates exceeding the upper confidence band were the exception rather than the rule. Figures 3 and 4, which show the drug/control response ratios in the unpunished component for R11 following pentobarbital and ethanol administration, represent the more common effects of these drugs on unpunished responding.

Additional analyses were conducted in an attempt to understand the nature of the pentobarbital-produced increases in the unpunished component. It was observed through examination of the cumulative records that the rate of responding on control days decreased to near zero towards the end of each unpunished component for some of the subjects. This trend was especially prevalent in animals R9 and R12. This trend was quantified through analysis of the cumulative records.

Table 15. Average Drug/Control Response Ratios in the Unpunished Component - Ethanol Regimen

Subject	R9	R10	R11	R12
Dose Level (g/kg)				
0.5	0.93	1.18	0.83	1.15
0.75	-	-	0.77	0.99
1.0	0.91	1.26	0.56*	0.66
1.25	-	-	0.82	0.72
1.50	1.02	0.96	1.03	0.90
2.0	0.79	0.95	0.84	0.89
2.5	0.43*	0.79	0.78	0.59
4.0	0.61	0.25*	0.66*	0.35*

* Denotes a drug effect on the response rate for a subject at a particular dose, as defined by ratios exceeding the upper or lower quasi-confidence bands.

Table 16. Average Drug/Control Response Ratios in the Unpunished Component - Pentobarbital Regimen

Subject	R9	R10	R11	R12
Dose Level (mg/kg)				
8	0.92	1.04	1.16	1.19
10	0.93	1.45	0.88	1.01
12	1.30	1.03	0.91	1.54*
16	0.83	0.63	0.66	1.76*
20	0.61	0.21*	0.07*	0.29*

* Denotes a drug effect on response rate for a subject at a particular dose, as defined by ratios exceeding the upper or lower quasi-confidence bands.

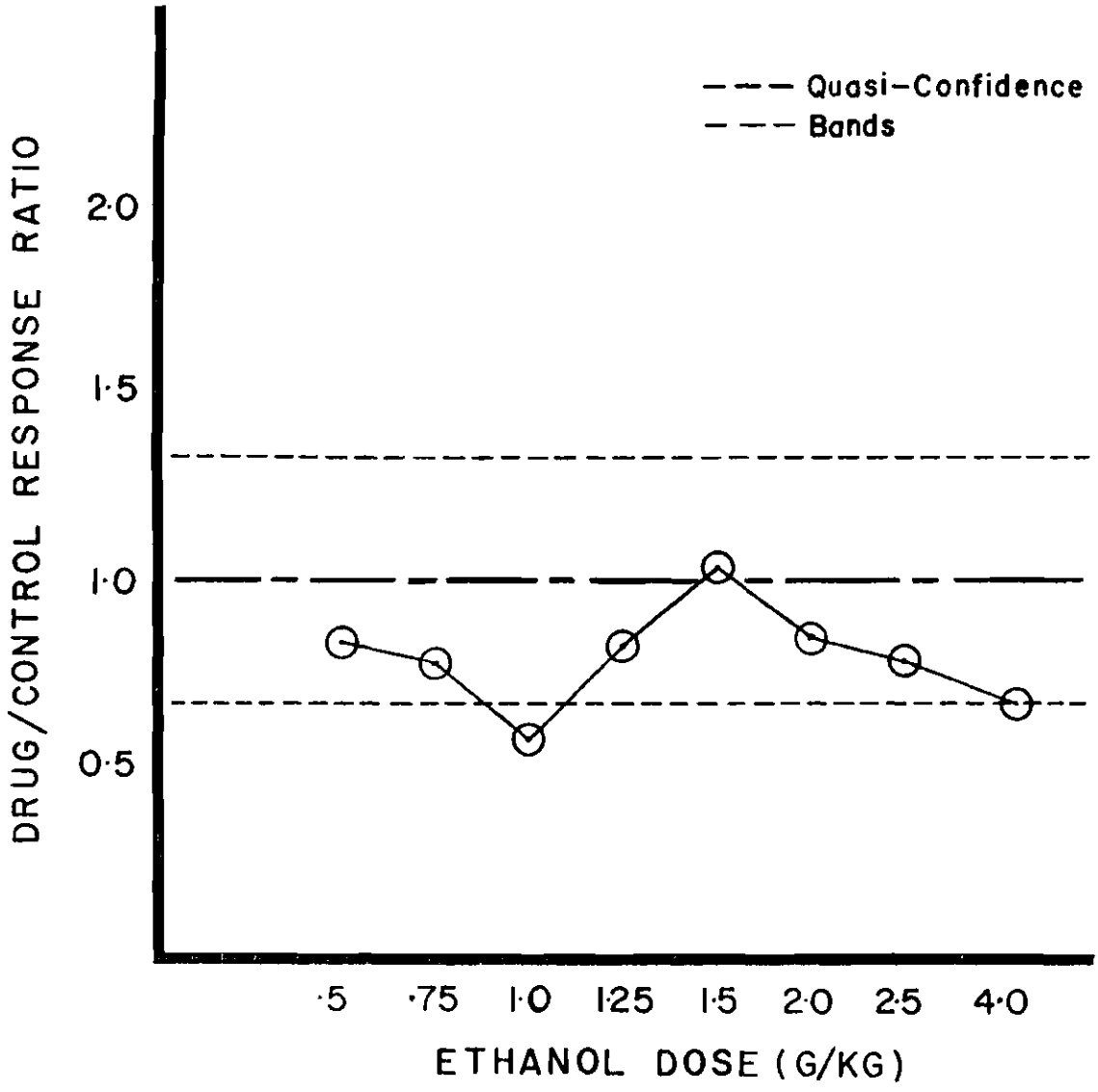

Figure 3· Drug/Control Response Ratio in the Unpunished Component for Subject RII—Ethanol Regimen

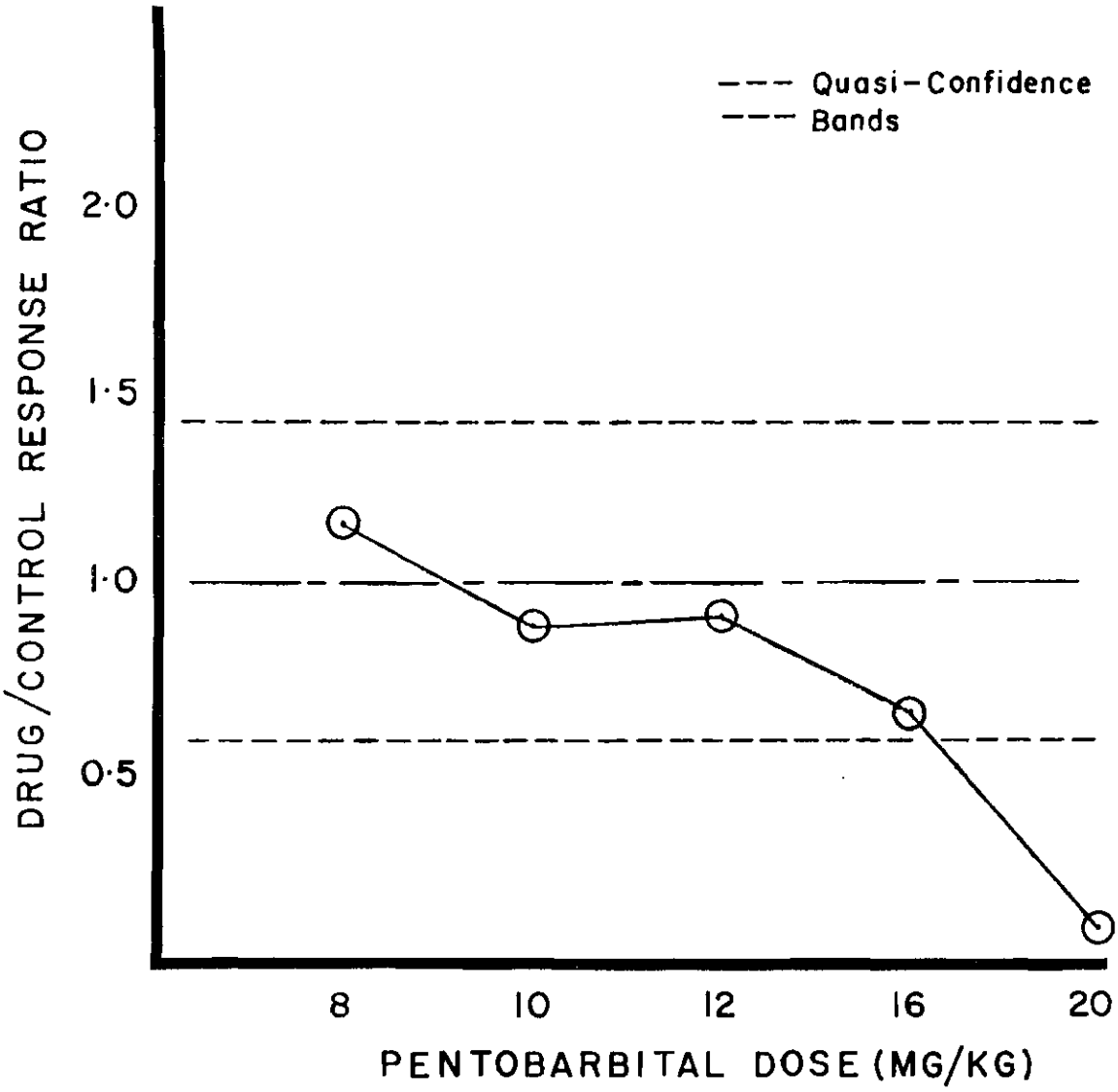

Figure 4· Drug/Control Response Ratio in the Unpunished Component for Subject RII- Pentobarbital Regimen

For each control session preceding a pentobarbital session, responding in the 5-minute unpunished components was analyzed. The cumulative record of each 5-minute component was divided into two halves. The rate in the first half was designated r_I, and the rate in the second half, preceding the onset of punishment, was designated r_{II}. These two rates were summed over each control session, and the ratio $\sum r_{II}/\sum r_I$ was computed for each session. An average of these ratios over the ten water control sessions was computed for each subject. Given that the rate in the second half of the unpunished components was the same as the rate in the first half, the ratio for each subject should be equal to one. The average ratios for R9, R10, R11 and R12 were 0.48, 0.65, 0.88 and 0.60, respectively. These average ratios show that the rate of responding tapers off during the second half of the unpunished component. As the onset of the punished component approaches, response rate decreases.

Computing this same ratio, $\sum r_{II}/\sum r_I$ for the unpunished component for the pentobarbital sessions, average ratios of 0.59, 0.87, 0.90 and 0.81 were obtained for R9, R10, R11 and R12, respectively. Comparing these latter ratios with those already listed for water, it can be seen that pentobarbital increases the ratios substantially for subjects R9, R10 and R12, but not for R11. However, the rate of responding for R11 in the second half of the

unpunished component, r_{II}, on the control days was little depressed, as shown by the relatively high r_{II}/r_I ratios ($\sum r_{II}/\sum r_I = 0.88$). The moderate increase in the average ratio in the pentobarbital sessions for R9, R10 and R12 indicates that any increases in unpunished responding are possibly due to increases in rate in the second half of the unpunished component. If increases in the unpunished component following pentobarbital were primarily due to increases in r_I, the ratio would decrease on the pentobarbital days.

However, the possibility still remains that increases in the r_{II}/r_I ratio reflect decreases in r_I rather than increases in r_{II}. To assess this possibility, two other ratios were computed at each dose of pentobarbital. These ratios are: (1) $\sum r_{I_{DRUG}}/\sum r_{I_{CONTROL}}$ and (2) $\sum r_{II_{DRUG}}/\sum r_{II_{CONTROL}}$. Ratios considerably larger than one indicate increases produced by pentobarbital in the unpunished rate, while ratios much less than one indicate decreases. Ratios equal to one indicate that pentobarbital had no effect. Table 17 gives these ratios for all subjects. Notice that the $\sum r_{I_D}/\sum r_{I_C}$ ratio is less than one for subject R10. This indicates that the previously noted increase in the r_{II}/r_I ratio for R10 following pentobarbital administration was primarily due to a decrease in r_{I_D} rather than an

Table 17. Average Drug/Control Ratios for Each Half of the Unpunished Components - **Pentobarbital**

	Subject			
	R9	R10	R11	R12
$\Sigma r_{I_D} / \Sigma r_{I_C}$	1.01	0.87	0.78	1.11
$\Sigma r_{II_D} / \Sigma r_{II_C}$	1.55	1.04	0.83	1.87

increase in r_{II_D}. On the other hand, for subjects R9 and R12, this previously noted increase was primarily due to large drug-produced increases in r_{II}. Notice in Table 17 that both ratios for R11 are less than one. For this animal, pentobarbital produced approximately equal decreases in responding in both halves of the unpunished component. Observe that the largest r_{II_D}/r_{II_C} ratio was obtained for subject R12, the subject for which pentobarbital increased overall unpunished rate. A moderate increase in this ratio was also noted for R9. However the large variability in the control rate possibly masked the effects on overall unpunished rate for this subject. The r_{I_D}/r_{I_C} ratios for for both R9 and R12 were somewhat closer to one, indicating that pentobarbital had little effects on the first half of the unpunished component. For R10, the decreases in r_I following pentobarbital were more than enough to offset the slight increases in r_{II}. Therefore, no increase in unpunished response rate was observed in R10 following pentobarbital administration.

Effects of Pentobarbital and Ethanol on IRT's in the Punished Component

For those doses of pentobarbital and ethanol that increased punished responding most in each subject, relative frequency of responses in each IRT response bin was calculated. There were ten response bins, each bin represent- a different IRT range. Bins one through nine each had a

range of one second. For example, the frequency of IRT's less than or equal to one second was recorded in bin one. Bin two contained the frequency of IRT's greater than one second but less than or equal to two seconds. In bin nine were IRT's greater than eight seconds but less than or equal to nine seconds. The last bin was reserved for a frequency count of the IRT's greater than nine seconds. Those IRT's in bin ten were designated as long IRT's and in bin one as short IRT's. The IRT's in the remaining bins were designated as medium length IRT's. To calculate relative frequency of different length IRT's, the frequency of the IRT length in which there was an interest was divided by the total count of IRT's in all ten IRT response bins. The average relative frequency of short, long and medium range IRT's in the punishment component for the drug and control days is given in Table 18. An increment or decrement of 0.10 in relative frequency of short, medium or long IRT's was considered an effect.

For subjects R9, R11 and R12, pentobarbital decreased the relative frequency of long IRT's and increased the frequency of medium length IRT's in the punished component. In addition, pentobarbital increased the frequency of short IRT's for R12. The 2.0g/kg doses of ethanol also decreased the relative frequency of long IRT's, while increasing the frequency of medium length IRT's. No changes in the IRT distribution were found for R10. For

Table 18. Relative Frequency of Different Length IRT's in the Punished Component for Control and Drug Sessions

	IRT Length (Relative Frequency) Short	Medium	Long
Subject R9			
Water Control	.0139	.0267	.9594
Pentobarbital (20mg/kg)	.0145	.3476	.6379
Sucrose (1.0g/kg)	.0000	.0218	.9782
Ethanol (1.0g/kg)	.0000	.1035	.8968
Subject R10			
Water Control	.0510	.5895	.3595
Pentobarbital (12mg/kg)	.1453	.5606	.2941
Subject R11			
Water Control	.0457	.2594	.6949
Pentobarbital (8mg/kg)	.0747	.5075	.4178
Sucrose (2.0g/kg)	.0280	.2617	.7103
Ethanol (2.0g/kg)	.0229	.6107	.3664
Subject R12			
Water Control	.0257	.0256	.9487
Pentobarbital (16mg/kg)	.3419	.6323	.0258
Sucrose (2.0g/kg)	.0227	.0682	.9091
Ethanol (2.0g/kg)	.0473	.2003	.7524

subject R9, the 1.0g/kg dose of ethanol also failed to modify the relative frequency of different length IRT's.

Effects of Pentobarbital and Ethanol on IRT's in the Unpunished Component

As shown in Table 19, the tendency of pentobarbital and ethanol was to either decrease the length of the IRT's in the unpunished component or have no effect on them. The only exception to this tendency was the pentobarbital-produced increase in the frequency of short IRT's and the accompanying decrease in the frequency of long IRT's for R12. For R9, pentobarbital produced a shift from more short IRT's to more long IRT's. Similarly ethanol produced a shift from more short IRT's to more medium length IRT's for subject R11. No additional effects on IRT frequency were observed.

Table 19. Relative Frequency of Different Length IRT's in the Unpunished Component for Control and Drug Sessions

	IRT Length (Relative Frequency) Short	Medium	Long
Subject R9			
Water Control	.4646	.3101	.2253
Pentobarbital (20mg/kg)	.2387	.3590	.4023
Sucrose (1.0g/kg)	.6933	.1780	.1287
Ethanol (1.0g/kg)	.6728	.1631	.1641
Subject R10			
Water Control	.4924	.3632	.1444
Pentobarbital (12mg/kg)	.4678	.3677	.1645
Subject R11			
Water Control	.3893	.4072	.2035
Pentobarbital (8mg/kg)	.3687	.4464	.1849
Sucrose (2.0g/kg)	.4424	.4304	.1272
Ethanol (2.0g/kg)	.3323	.5431	.1246
Subject R12			
Water Control	.3331	.5173	.1496
Pentobarbital (16mg/kg)	.4999	.4802	.0199
Sucrose (2.0g/kg)	.3754	.4952	.1294
Ethanol (2.0g/kg)	.3396	.5255	.1859

CHAPTER V

DISCUSSION

The results demonstrate that ethanol administered orally may produce increases in punished responding at certain doses. This result is in agreement with the findings of Vogel-Sprott (1967), Freed (1972), and McMillan & Leander (1975). **Moreover, the present study extends** the findings of these studies to a wider range of doses. As shown in Table 8, the dose effective in increasing punished rate ranged from 1.0g/kg to 2.5g/kg. Increases for two of the four subjects were obtained for the 2.0 and 2.5g/kg doses, the maximum effect occurring for the 2.0g/kg dose. From previous studies on punishment (Vogel-Sprott, 1967; McMillan & Leander, 1975) and the Fish & Nelson (1942) data, it was expected that the maximum effect would be produced by the 1.0g/kg dose of ethanol. Even though the present study administered ethanol orally, as did Vogel-Sprott (1967) and McMillan & Leander (1975), the concentration of the ethanol solution in weight per volume (w/v) of all doses for the present study was probably not equivalent to that for previous studies. Since the rate at which ethanol is absorbed into the blood is related to the concentration of the ethanol solution, the difference in w/v

of ethanol might account for the difference in effective dose level. Other procedural differences in the present study that might account for the difference in the dose producing maximum effects in rate include the shock intensities used, the non-pairing of reinforcement and punishment, and the administration of each dose more than once.

For three of the four subjects, punished rate was increased by at least one dose level of ethanol, as shown in Table 8. However, response rate was not increased at any dose of ethanol for R10. This lack of effects of ethanol for R10 may be due to the fact that the punished rate was a larger proportion of the unpunished rate for this subject. Whatever the reason for the lack of effects produced by ethanol, the same result was not observed for R10 following pentobarbital administration. As seen in Table 9, two of five doses of pentobarbital produced significant increases in punished rate for this subject. It is of some interest that R10 was the only subject for which the 8 and 16mg/kg dose of pentobarbital produced no effects.

The 10 and 12mg/kg doses of pentobarbital consistently produced increases in punished responding for all subjects. The increases in punished responding were generally larger than those produced by ethanol. The magnitude of the effect of pentobarbital relative to the magnitude and variability of effects produced by ethanol may itself account for the consistency of the effects of pentobarbital across studies

and the inconsistency of ethanol effects across studies.

In contrast to the punished component, response rate in the unpunished component was either not affected or was decreased by ethanol. These results are in accord with those found by Barry et al. (1963) and Geller & Croy (1974), but disagree with Freed's (1972) results. For those doses of pentobarbital that increased punished responding, unpunished responding was for the most part unaffected. Similar results were obtained by McMillan (1973 a). For subject R12, pentobarbital increased unpunished responding at certain dose levels. The analysis of the effects of pentobarbital on unpunished responding demonstrated that the increases in the unpunished rate for this subject were primarily due to restoration of suppressed responding in the latter half of the unpunished components. This result indicates that the punishment contingency was interacting with responding in the last half of the unpunished component. The temporal proximity of the second half of the unpunished component with the punishment contingency led to anticipatory decreases in rate of responding. Hanson et al. (1967) also obtained increases in unpunished responding following 2.5, 5.0, 7.5 and 10mg/kg doses of pentobarbital administered orally. Hanson and his associates also employed a multiple schedule in which the punished component immediately followed the unpunished component. Thus, Hanson's results may also be a function of the interaction of

punishment with unpunished responding. These results suggest that if a multiple schedule is to be used to simultaneously assess the effects of drugs on punished and unpunished responding, then a time-out in which responding has no consequences should follow the unpunished component and precede the punished component.

Both pentobarbital and ethanol had effects on the IRT distribution for punished responding. Pentobarbital resulted in a shift towards shorter IRT's in the punished component for all subjects except R10. The increase in short IRT's (≤1 sec.) produced by pentobarbital (16mg/kg) for subject R12 indicates an increase in bursts of responses. For subjects R11 and R12, ethanol increased the proportion of medium length IRT's at the expense of long IRT's. This ethanol-produced increase in the proportion of shorter IRT's conflicts with the findings of Hendry and Van Toller (1964), who found that the only effect that ethanol had on IRT length was to increase the length of the long IRT's. For the IRT measure as for the rate measure, ethanol was less consistent in producing clear effects on punished responding than was pentobarbital.

In contrast to the shift towards shorter IRT's in the punished component, ethanol and pentobarbital generally increased the proportion of long IRT's in the unpunished component. The exception to this general finding is that the 16mg/kg dose of pentobarbital increased the proportion

of medium length IRT's while decreasing the proportion of long IRT's for R12. This shift toward shorter IRT's parallels the shift in the punished component and most likely reflects the interactive effects of punishment on the second half of the unpunished component.

The present study shows that orally administered ethanol occasionally produces increases in responding suppressed by punishment within a dose range of 1.0g/kg to 2.5g/kg. While the present study used rats as subjects, similar effects have been shown in pigeons (McMillan & Leander, 1975) and humans (Vogel-Sprott, 1967). Though the oral method of ethanol administration may not be necessary for obtaining increases in punished responding, the administration of a wide range of low doses of ethanol does seem to be necessary. In addition to the dose level in weight per kilogram of body weight, it is suggested that the weight per volume of the drug solution be systematically varied within a dose level in conjunction with the length of the experimental session.

Future studies that propose to evaluate the effects of ethanol on punished responding should avoid pairing the punishing stimulus with reinforcement, thereby not attaching additional properties to the punisher. It would also be wise to administer each dose of ethanol as many times as practically feasible. Special attention should be given to parameters that affect the rate at which a drug enters the

blood and the peak concentration in the blood. Such parameters include route of administration, dose, and the concentration of the drug solution.

Finally, it is important to note that the present study was not without its difficulties and limitations. Although the multiple VI 90-sec VI 90-sec schedule allowed rate to vary over a wide range without affecting the number of reinforcements available, the low response rates resulted in a decrease in the number of reinforcements obtained in the punished component. Since the number of reinforcements obtained were not equal in the two components, it cannot be stated with certainty that the ultimate decrease in rate in the punished component was entirely due to the shock dependency. Thus the increase in punished rate following drug administration may reflect an increase in rate suppressed by a combination of shock and a diminished number of reinforcements. In addition, the response rates for two of the four subjects did not stabilize and were quite variable when the drug regimen began. This variability could mask the small magnitude effects produced by ethanol and may have been a contributing factor in the failure of ethanol to significantly increase punished responding in subject R10. However, even given these limitations, the production of increases in punished responding following both pentobarbital and ethanol, and the greater magnitude of effects produced by pentobarbital have been established with reasonable certainty.

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